

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
22 April 2004 (22.04.2004)

PCT

(10) International Publication Number
WO 2004/033465 A1

(51) International Patent Classification⁷: **C07D 513/20**,
A61K 31/429, A61P 35/00, C07F 7/18 // (C07D 513/20,
319:00, 311:00, 277:00)

(74) Agents: **BRANTS, Johan, Philippe, Emile et al.**; De
Clercq, Brants & Partners, E. Gevaertdreef 10a, B-9830
Sint-Martens-Latem (BE).

(21) International Application Number:
PCT/EP2003/011194

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK,
MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT,
RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR,
TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(22) International Filing Date: 9 October 2003 (09.10.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
02447192.2 9 October 2002 (09.10.2002) EP
60/420,067 21 October 2002 (21.10.2002) US

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,
SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM,
GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(71) Applicant (*for all designated States except US*): **UNIBIO-
SCREEN S.A.** [BE/BE]; Avenue J. Wybran 40, B-1070
Bruxelles (BE).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **VAN QUAQUE-
BEKE, Eric** [BE/BE]; Chaussée de Roodebeek 479/4,
B-1200 Woluwe-Saint-Lambert (BE). **BRAEKMAN,
Jean-Claude** [BE/BE]; Avenue Sainte Thérèse 7, B-1640
Rhode-Saint-Genèse (BE). **SIMON, Gentiane** [BE/BE];
Avenue du Docteur Roux 36, B-1070 Bruxelles (BE).
GUISSOU, Pierre [BF/BF]; 01 PB 1806, -- Ouagadougou
(BF). **NACOUлма, Odile, Germaine** [BF/BF]; 01
BP 1938, -- Ouagadougou (BF). **DEWELLE, Janique**
[BE/BE]; Rue du Pachy Couche 35, B-6238 Luttre (BE).
DARRO, Francis [FR/BE]; 143, Rue de la Pêcherie, Boîte
3, B-1180 Uccle (BE). **KISS, Robert** [BE/BE]; Henri
Consciencestraat 34-b3, B-1600 Sint-Pieters-Leeuw (BE).

Declaration under Rule 4.17:

— *of inventorship (Rule 4.17(iv)) for US only*

Published:

— *with international search report*
— *before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments*

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: **2'' OXO-VORUSCHARIN AND DERIVATIVES THEREOF**

(57) Abstract: The present invention relates to the novel compound 2'' oxo-voruscharin and derivatives. In addition, the present invention relates to pharmaceutical compositions comprising the novel 2'' oxo-voruscharin or derivatives. The present invention further relates to the 2'' oxo-voruscharin and derivatives for use as a medicament and for use in the preparation of a medicament for treating cancer. The present invention also relates to a method of treating cancer.

WO 2004/033465 A1

INTERNATIONAL SEARCH REPORT

International Application No.
PCT/EP 03/11194

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D513/20 A61K31/429 A61P35/00 C07F7/18
//(C07D513/20,319:00,311:00,277:00)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 52562 A (VERKAIK) 26 November 1998 (1998-11-26) cited in the application page 4, line 6 - line 12	1,27
X	CHEUNG, H. T. ANDREW ET AL: "Cardenolide glycosides of the Asclepiadaceae. New glycosides from Asclepias fruticosa and the stereochemistry of uscharin, voruscharin, and calotoxin" JOURNAL OF THE CHEMICAL SOCIETY, PERKIN TRANSACTIONS 1: ORGANIC AND BIO-ORGANIC CHEMISTRY (1972-1999) (1983), (12), 2827-35 , XP002271160 page 2828, compounds 1b, 3b, 3c	1

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

23 February 2004

Date of mailing of the international search report

04/03/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Alfaro Faus, I

INTERNATIONAL SEARCH REPORT

Intern. Application No.
PCT/JP 03/11194

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 645 988 A (VANDE WOUDE ET AL.) 8 July 1997 (1997-07-08) columns 23-24, table 6, compound 650362	1,27

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/11194

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claim 29 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Publication No
PCT/EP 03/11194

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9852562	A	26-11-1998	AT 210978 T	15-01-2002
			AU 7543198 A	11-12-1998
			BR 9809159 A	01-08-2000
			DE 69803059 D1	31-01-2002
			DE 69803059 T2	22-08-2002
			EP 0983063 A1	08-03-2000
			WO 9852562 A1	26-11-1998
			JP 2001527569 T	25-12-2001
			NZ 501421 A	25-08-2000
			US 6342490 B1	29-01-2002
US 5645988	A	08-07-1997	US 6150398 A	21-11-2000
			AU 2005692 A	21-12-1992
			WO 9219765 A1	12-11-1992